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FILE 'HOME' ENTERED AT 14:15:02 ON 09 FEB 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:15:16 ON 09 FEB 2007
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DICTIONARY FILE UPDATES: 8 FEB 2007 HIGHEST RN 920112-67-0

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=> screen 1006

L1 SCREEN CREATED

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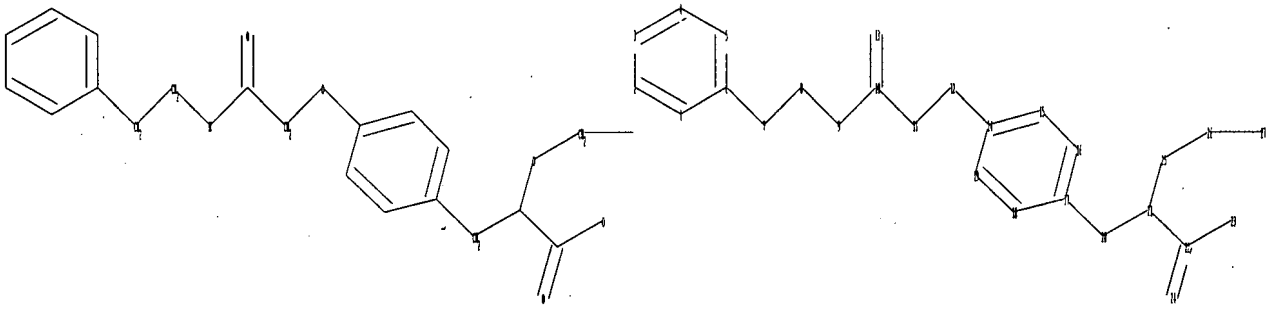

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ring nodes :
1 2 3 4 5 6 14 15 16 17 18 19
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exact/norm bonds :
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exact bonds :
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normalized bonds :
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Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:CLASS 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom
27:Atom

L2 STRUCTURE UPLOADED

=> que L2 AND L1

L3 QUE L2 AND L1

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L1 HAS NO ANSWERS
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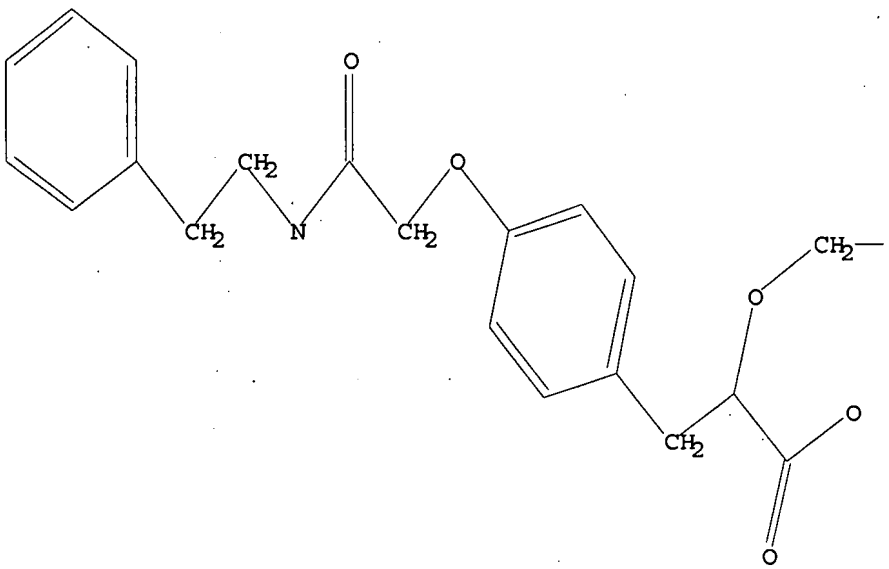
L2 HAS NO ANSWERS
L2 STR



Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED -      716 TO ITERATE

100.0% PROCESSED      716 ITERATIONS                          19 ANSWERS
SEARCH TIME: 00.00.01

L4            19 SEA SSS FUL L2

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                               172.10     172.31

FILE 'CAPLUS' ENTERED AT 14:16:03 ON 09 FEB 2007
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FILE LAST UPDATED: 8 Feb 2007  (20070208/ED)

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=> s L4
L5            9 L4

=> d L5 1-9 bib abs

L5   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2007:61504  CAPLUS
DN   146:142376
TI   Preparation of phenylpropionic acid derivatives and pharmaceutical
     compositions thereof
IN   Bjoerk, Seth
PA   Astrazeneca AB, Swed.
SO   PCT Int. Appl., 57pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2007008156        A1    20070118    WO 2006-SE864           20060710
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             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
             SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
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US, UZ, VC, VN, ZA, ZM, ZW
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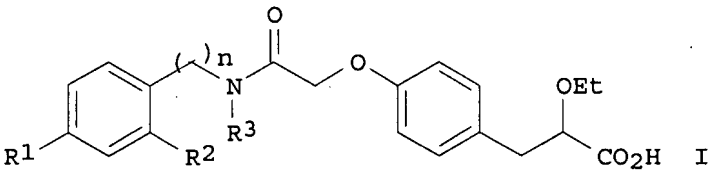
PRAI SE 2005-1644 A 20050711
GI



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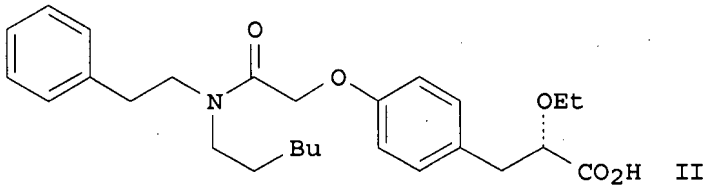

II

AB The title phenylpropionic acid derivs. I [wherein n = 1-2; R1 = H, Cl, CF3, or OCF3; R2 = H or F; R3 = alkyl] or tert-butylamine salts thereof were prepared as PPAR active compds. for treatment of metabolic syndrome including type 2 diabetes mellitus (no data). For example, II and II•tert-butylamine were prepared in a multi-step synthesis. Pharmaceutical compns. were described.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:605020 CAPLUS
DN 145:83115
TI Preparation of tris(hydroxymethyl)methylamine and ethanolamine salts of (2S)-2-ethoxy-3-(4-{2-[hexyl(2-phenylethyl)amino]-2-oxoethoxy}phenyl)propanoic acid for treating lipid disorders
IN Booth, Rebecca J.; Dahlstroem, Mikael
PA AstraZeneca AB, Swed.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006065214	A1	20060622	WO 2005-SE1916	20051214

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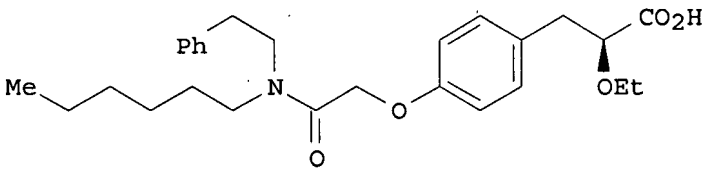
KG, KZ, MD, RU, TJ, TM
PRAI SE 2004-3072 A 20041216
GI



I

AB The invention relates to a compound selected from one or more of the following: a tris(hydroxymethyl)methylamine salt or an ethanolamine salt of title compound I or a pharmaceutical composition comprising the compound
Thus I
was prepared in 4 steps from Et (S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate, benzyl bromoacetate, and N-hexyl-2-phenylethylamine. X-ray powder diffration patterns for bot salts of I are given. Both salts have an EC50 of less than 0.5 μmol/l for PPARα.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1335635 CAPLUS
DN 144:69628
TI Preparation of phenoxyacetamide derivatives as modulators of peroxisome proliferator-activated receptors (PPAR)
IN Alstermark, Eva-Lotte Lindstedt; Olsson, Anna Christina; Li, Lanna
PA Swed.
SO U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 499,261.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005282822	A1	20051222	US 2004-26806	20041230
WO 2003051821	A1	20030626	WO 2002-GB5738	20021218
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CN 1896045	A	20070117	CN 2006-10007173	20021218
WO 2004056748	A1	20040708	WO 2003-GB5602	20031219
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WO 2004113270 A2 20041229 WO 2004-EP6597 20040617

WO 2004113270 A3 20050331

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EP 1676833 A1 20060705 EP 2006-5766 20040617

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JP 2006298925 A 20061102 JP 2006-139673 20060519

PRAI SE 2001-4334 A 20011219

WO 2002-GB5738 W 20021218

WO 2002-GB5744 A 20021218

GB 2002-29931 A 20021221

GB 2003-14079 A 20030618

WO 2003-GB305602 A 20031219

WO 2004-EP6597 A 20040617

US 2005-499261 A2 20050304

CN 2002-828123 A3 20021218

JP 2003-552709 A3 20021218

JP 2003-552710 A3 20021218

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JP 2006-515989 A3 20040617

OS MARPAT 144:69628

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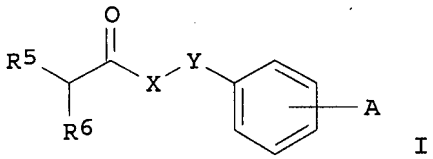

I

AB The phenyl-, phenoxy-, or phenylthioalkanamidetitle compds., (in particular phenoxyacetamide derivs.) (I) [A is situated in the ortho, meta or para position and represents CR3R4CR1R2COR, CR3:CR1COR (wherein R = H, alkyl, (un)substituted HO or NH2; R1 = alkyl, aryl, alkenyl, alkynyl, or when A is CR3R4CR1R2COR, R1 can also be cyano, (un)substituted HO, SH, OCONH2, SO2NH2, CO2H, etc.; R2 = H, halogen, alkyl, aryl, alkylaryl; R3, R4 = H, alkyl, aryl, alkylaryl); Y = O, S, a single bond; n = an integer of 1-4; X = alkyl; R5, R6 = H, each (un)substituted C1-13 alkyl, C2-10 alkenyl, or C2-10 alkynyl; or R5, R6 = each (un)substituted C3-8

cycloalkyl, C3-C8 cycloalkenyl, aryl, heterocyclyl, or heteroaryl; or R5 and R6 together with the nitrogen atom to which they are attached form a single or a fused heterocyclic system] are prepared These compds. are useful in treating clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance, and other manifestations of the metabolic syndrome. Thus, a solution of 0.598 g N-butyl-N-[2-fluoro-4-(trifluoromethyl)benzyl]amine and 0.593 g [4-((2S)-2,3-diethoxy-3-oxopropyl)phenoxy]acetic acid in 20 mL CH2Cl2 was treated with 0.80 mL N,N-diisopropylethylamine and 0.674 g O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate and the reaction mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., 74% Et (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate (II). A solution of 0.748 g II in 70 mL MeCN was treated with 35 mL 0.10 M LiOH and the reaction mixture was stirred at room temperature overnight, neutralized with 5% HCl, concentrated, acidified with 5% HCl, and extracted with EtOAc to give 97% (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid (III). III showed EC50 of 0.001 μmol/L for human PPARα.

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1154649 CAPLUS
DN 142:93514
TI Preparation of phenylpropanoic acid derivatives as PPARα agonists
IN Li, Lanna; Lindstedt-Alstermark, Eva-Lotte; Olsson, Christina
PA Astrazeneca Ab, Swed.
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

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	CA 2528234	A1	20041229	CA 2004-2528234	20040617
	US 2005148656	A1	20050707	US 2003-518777	20040617
	EP 1675820	A2	20060705	EP 2004-740044	20040617
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	CN 1835913	A	20060920	CN 2004-80023304	20040617
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	US 2005282822	A1	20051222	US 2004-26806	20041230
	NO 2005005892	A	20060106	NO 2005-5892	20051212
	JP 2006298925	A	20061102	JP 2006-139673	20060519
	US 2006258866	A1	20061116	US 2006-477168	20060628
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	SE 2001-4334	A	20011219		

	WO 2002-GB5738	W	20021218
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	GB 2002-29931	A	20021221
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OS MARPAT 142:93514

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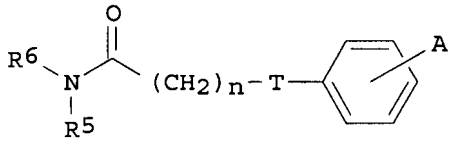

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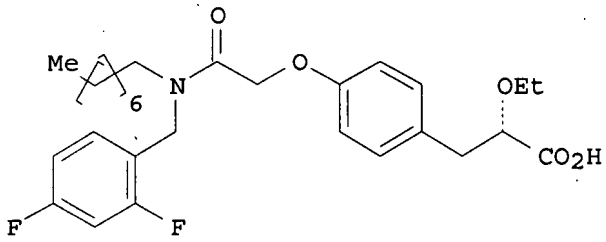

II

AB Title compds. represented by the formula I [wherein A = CR3(R4)CR1(R2)COR or C(R3):C(R1)COR; R = H, alkoxy, (alkyl)aryloxy, amino, etc.; R1 = alkyl, aryl, alkenyl, alkynyl, etc.; R2 = H, halo, alkyl, (alkyl)aryl; R3, R4 = independently H, alkyl, (alkyl)aryl; T = O, S or a single bond; n = 1-4; R5, R6 = independently selected substituent comprising C, H, N, O, S, Se, P or halo; with provisos; optical isomers and racemates thereof as well as pharmaceutically acceptable salts, prodrugs, solvates and crystalline forms thereof] were prepared as PPARα agonists. For example, II was given in a multi-step synthesis starting from the reaction of 2,4-difluorobenzylamine with octanoic acid. I had EC50 values of less than 0.1 μmil/L for PPARα and showed the ration of the EC50(PPARγ) with EC50(PPARα) is greater than 150:1. Thus, I and their pharmaceutical compns. are useful for the treatment of clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance (no data).

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:1127321 CAPLUS

DN 142:49239

TI Pharmaceutically useful salts (2S)-2-ethoxy-3-(4-{2[hexyl(2-phenylethyl)amino]-2-oxoethoxy}phenyl)propanoic acid, preparation thereof, and therapeutic use

IN Ragnar, Ralf; Stahle, Erica

PA Astrazeneca AB, Swed.

SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110985	A1	20041223	WO 2004-SE965	20040616

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2004247611	A1	20041223	AU 2004-247611	20040616
CA	2527608	A1	20041223	CA 2004-2527608	20040616
EP	1638921	A1	20060329	EP 2004-736956	20040616
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR	2004011455	A	20060718	BR 2004-11455	20040616
CN	1805922	A	20060719	CN 2004-80016838	20040616
JP	3836498	B2	20061025	JP 2006-517040	20040616
JP	2006527767	T	20061207		
US	2006194879	A1	20060831	US 2005-560127	20051209
NO	2005005923	A	20060106	NO 2005-5923	20051213
PRAI GB	2003-14136	A	20030618		
WO	2004-SE965	W	20040616		

AB The invention discloses a calcium or magnesium salt of (2S)-2-ethoxy-3-(4-{2[hexyl(2-phenylethyl)amino]-2-oxoethoxy}phenyl)propanoic acid. Compds. of the invention (preparation included) may be used to treat e.g. dyslipidemia and type 2 diabetes.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1127320 CAPLUS
DN 142:49238
TI Pharmaceutically useful salts of (2S)-2-ethoxy-3-[4-(2-(hexyl(2-phenylethyl)amino)-2-oxoethoxy)phenyl]propanoic acid, their preparation, and their therapeutic use
IN Aurell, Carl-Johan; Dahlstroem, Mikael; Lindstedt-Alstermark, Eva-Lotte; Minidis, Anna; Ohlsson, Bengt; Stahle, Erica
PA Astrazeneca AB, Swed.
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110984	A1	20041223	WO 2004-SE964	20040616
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004247610	A1	20041223	AU 2004-247610	20040616
	CA 2528932	A1	20041223	CA 2004-2528932	20040616
	EP 1638922	A1	20060329	EP 2004-749009	20040616
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1809529	A	20060726	CN 2004-80016948	20040616

	BR 2004011525	A	20060801	BR 2004-11525	20040616
	JP 3822900	B2	20060920	JP 2006-517039	20040616
	JP 2006527766	T	20061207		
	NO 2005005922	A	20060106	NO 2005-5922	20051213
	US 2006142389	A1	20060629	US 2005-560657	20051213
PRAI	GB 2003-14129	A	20030618		
	WO 2004-SE964	W	20040616		

AB The invention discloses salts of (2S)-2-ethoxy-3-[4-(2-(hexyl(2-phenylethyl)amino)-2-oxoethoxy)phenyl]propanoic acid e.g. the L-arginine salt. Preparation of compds. of the invention is described. The compds. of the invention are useful in the treatment of e.g. dyslipidemias and other manifestations of the metabolic syndrome.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1127318 CAPLUS
DN 142:56001
TI Preparation of (2S)-3-(4-{2-[amino]-2-oxoethoxy}phenyl)-2-ethoxypropanoic acid derivatives
IN Aurell, Carl-Johan; Macedo, Emmanuel; Minidis, Anna; Yousefi-Salakdeh, Esmail
PA Astrazeneca Ab, Swed.
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110982	A1	20041223	WO 2004-SE966	20040616
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004247612	A1	20041223	AU 2004-247612	20040616
	CA 2528933	A1	20041223	CA 2004-2528933	20040616
	EP 1638920	A1	20060329	EP 2004-736958	20040616
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1809528	A	20060726	CN 2004-80017131	20040616
	BR 2004011558	A	20060801	BR 2004-11558	20040616
	JP 3822901	B2	20060920	JP 2006-517041	20040616
	JP 2006527768	T	20061207		
	NO 2005005924	A	20060105	NO 2005-5924	20051213
	US 2006142392	A1	20060629	US 2005-560764	20051213
PRAI	GB 2003-14134	A	20030618		
	WO 2004-SE966	W	20040616		

OS MARPAT 142:56001
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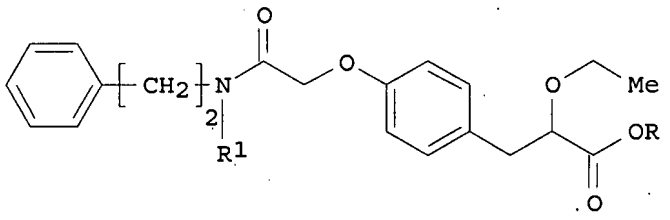

I

AB The present invention provides a process for preparation of the title compds. I (R = H, R1 = n-C6H13) by reacting I (R = H, or protecting group, R1 = H) with C6H13X (X = leaving group) in the presence of a base and inert solvent at a temperature in the range -25°C to 150°C and optionally, when OR represents a protecting group, removal of the protecting group.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:2837 CAPLUS
DN 140:59411
TI Preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X
IN Ferritto Crespo, Rafael; Martin, Jose Alfredo; Martin-Ortega, Finger Maria Dolores; Rojo Garcia, Isabel; Shen, Quanrong; Warshawsky, Alan M.; Xu, Yanping
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000789	A1	20031231	WO 2003-US16207	20030611
	WO 2004000789	A9	20040311		
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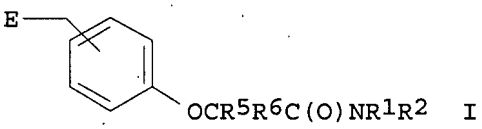
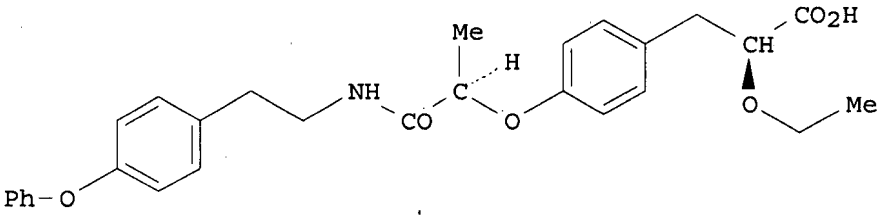
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2488972	A1	20031231	CA 2003-2488972	20030611
	AU 2003241579	A1	20040106	AU 2003-241579	20030611
	EP 1517882	A1	20050330	EP 2003-731326	20030611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003011834	A	20050412	BR 2003-11834	20030611
	CN 1662487	A	20050831	CN 2003-814173	20030611
	JP 2005529975	T	20051006	JP 2004-515700	20030611
	US 2006111406	A1	20060525	US 2004-517581	20041208
PRAI	US 2002-390102P	P	20020619		
	WO 2003-US16207	W	20030611		

OS MARPAT 140:59411
GI



I



II

AB The present invention is directed to phenoxyalkanamides (shown as I; variables defined below; e.g. II), compns., and their use as peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X. The binding and cotransfection efficacy values found for compds. of this invention that are useful for modulating a PPARα receptor are about <100 nM and >50%, resp. Although the methods of preparation are not claimed, .apprx.140 example prepns. of I are included. For example, II was prepared in 3 steps starting from (2S)-2-ethoxy-3-(4-hydroxyphenyl)propionic acid Me ester, (2S)-2-hydroxypropionic acid benzyl ester and involving intermediates (2S)-3-[4-[[(1R)-1-[(benzyloxy)carbonyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid Et ester and (2S)-3-[4-[((1R)-1-carboxyethyl)oxy]phenyl]-2-ethoxypropionic acid. For I: R1 = H, C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-4-alkyl, heteroaryl-C0-4-alkyl, aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-2-alkyl, arylheteroC1-C8alkyl, -CHC(O)C1-C4 alkoxy, C0-4-alkyl-C(O)heteroC1-C8alkyl, and -CH2C(O)-R15R16. R2 = C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, heteroC1-C6cycloalkylaryl, heteroC1-C6cycloalkylarylC1-C4alkyl, aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-C2-alkyl, arylheteroC1-C8alkyl, C0-C4-alkyl-C(O)heteroC1-C8alkyl, -CH(C(O)OCH3)benzyl, and -CH2C(O)R15''R16''. R1 and R2 together may form a heterocyclic ring which heterocyclic ring is (un)substituted with 1-3 substituents R1' and which heterocyclic ring is optionally fused with an aryl; E = C(R3)(R4)A, (CH2)nCOOR13, aryl-C0-C4-alkyl, thio-C1-C4-alkyl, thioaryl, arylC1-C4alkoxy, C1-C4alkoxy C1-C4alkyl, aminoaryl, and aminoC1-C4alkyl. R5 and R6 = H, C1-C8 alkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, C3-C6 cycloalkyl, aryl-C0-C2-alkyl, C3-C6 cycloalkyl-C0-2-alkyl, and -CH2C(O)R17R18.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:491168 CAPLUS
DN 139:69049
TI Preparation of substituted phenylpropionic acid derivatives as agonists to human peroxisome proliferator-activated receptor alpha (PPAR)
IN Alstermark Lindstedt, Eva-Lotte; Olsson, Anna Christina; Li, Lanna
PA Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003051821	A1	20030626	WO 2002-GB5738	20021218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

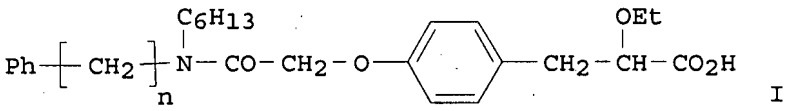
CA	2470491	A1	20030626	CA 2002-2470491	20021218
AU	2002366315	A1	20030630	AU 2002-366315	20021218
EP	1458673	A1	20040922	EP 2002-804964	20021218
EP	1458673	B1	20060906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR	2002014988	A	20041214	BR 2002-14988	20021218
HU	200402133	A2	20050228	HU 2004-2133	20021218
CN	1620422	A	20050525	CN 2002-828123	20021218
CN	1620423	A	20050525	CN 2002-828155	20021218
US	2005171204	A1	20050804	US 2003-499261	20021218
JP	2005526011	T	20050902	JP 2003-552709	20021218
JP	3784804	B2	20060614		
TW	253444	B	20060421	TW 2002-91136518	20021218
NZ	533276	A	20060428	NZ 2002-533276	20021218
TW	255807	B	20060601	TW 2002-91136519	20021218
AT	338743	T	20060915	AT 2002-804964	20021218
CN	1896045	A	20070117	CN 2006-10007173	20021218
ZA	2004004657	A	20050829	ZA 2004-4657	20040611
ZA	2004004658	A	20060222	ZA 2004-4658	20040611
NO	2004003023	A	20040715	NO 2004-3023	20040715
US	2005282822	A1	20051222	US 2004-26806	20041230
JP	2005336209	A	20051208	JP 2005-235794	20050816
JP	2006298924	A	20061102	JP 2006-123399	20060427

PRAI

SE	2001-4334	A	20011219
CN	2002-828123	A3	20021218
JP	2003-552709	A3	20021218
JP	2003-552710	A3	20021218
WO	2002-GB5738	W	20021218
WO	2002-GB5744	A	20021218
GB	2002-29931	A	20021221
GB	2003-14079	A	20030618
WO	2003-GB305602	A	20031219
WO	2004-EP6597	A	20040617
US	2005-499261	A2	20050304

OS MARPAT 139:69049

GI



I

AB The S enantiomer of I, n = 1 or 2, (C6H13 = hexyl) as well as their pharmaceutically acceptable salts, solvates, crystalline forms and prodrugs are synthesized using various solvents and in presence of charcoal-supported palladium catalyst. The utility of these compds. in clin. conditions such as lipid disorders (dyslipidemias) whether or not associated with insulin resistance and therapeutic and other pharmaceutical activities is also investigated. For example, (2S)-3-(4{2-[benzyl(hexyl)amino]-2-oxoethoxy}phenyl)2-ethoxypropionic acid was prepared in 58% yield via reaction of (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate and benzyl bromoacetate.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s (2S)-2-ethoxy-3-(4-{2-oxo-2-[(2-phenylethyl)amino]ethoxy}phenyl)-propanoic acid
MISSING TERM BEFORE '(2S'
Search expressions cannot begin with operators.

=> s 2-ethoxy-3-(4-{2-oxo-2-[(2-phenylethyl)amino]ethoxy}phenyl)propanoic acid
MISSING OPERATOR '-ETHOXY-3-(4-{2-OXO-2'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s phenethylamino ethoxy phenyl propanoic acid derivatives
          838 PHENETHYLAMINO
        42317 ETHOXY
       343103 PHENYL
          414 PHENYLS
       343381 PHENYL
                (PHENYL OR PHENYLS)
      1309164 PH
        10070 PHS
      1313504 PH
                (PH OR PHS)
      1566052 PHENYL
                (PHENYL OR PH)
         8991 PROPANOIC
      4311309 ACID
      1568117 ACIDS
      4812460 ACID
                (ACID OR ACIDS)
       340439 DERIVATIVES
      1134482 DERIVS
      1240054 DERIVATIVES
                (DERIVATIVES OR DERIVS)
L6          0 PHENETHYLAMINO ETHOXY PHENYL PROPANOIC ACID DERIVATIVES
                (PHENETHYLAMINO(W)ETHOXY(W)PHENYL(W)PROPANOIC(W)ACID(W)DERIVAT
                IVES)

=>

---Logging off of STN---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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
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FULL ESTIMATED COST                                41.29     213.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                -7.02      -7.02

STN INTERNATIONAL LOGOFF AT 14:20:59 ON 09 FEB 2007


Connecting via Winsock to STN
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Welcome to STN International! Enter x:x

LOGINID:ssptalxn1621

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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FILE LAST UPDATED: 8 Feb 2007  (20070208/ED)

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L1   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2006:453910  CAPLUS
DN   145:76018
TI   Identification of novel PPARα ligands by the structural modification
     of a PPARγ ligand
AU   Usui, Shinya; Fujieda, Hiroki; Suzuki, Takayoshi; Yoshida, Naoaki;
     Nakagawa, Hidehiko; Miyata, Naoki
CS   Graduate School of Pharmaceutical Sciences, Nagoya City University,
     Nagoya, Aichi, 467-8603, Japan
```
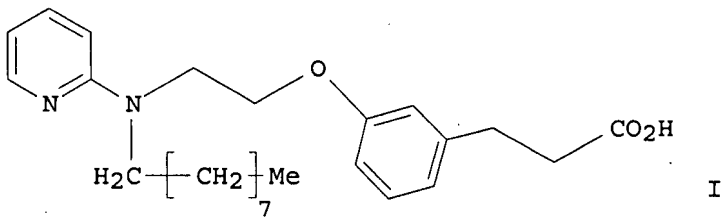

SO Bioorganic & Medicinal Chemistry Letters (2006), 16(12), 3249-3254
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
GI



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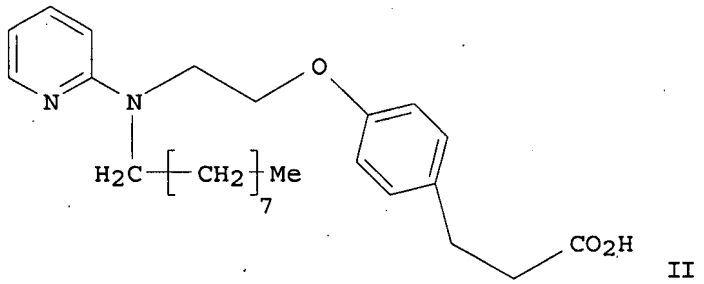
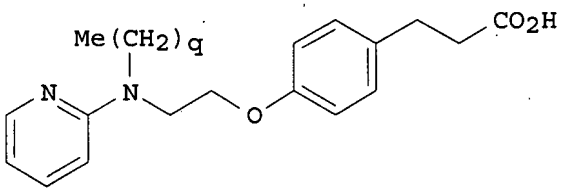


II

AB To develop novel PPARα ligands, the authors designed and synthesized several 3-{3-[2-(nonylpyridin-2-ylamino)ethoxy]phenyl} propanoic acid derivs. Compound (I), the meta isomer of a PPARγ agonist (II), has been identified as a PPARα ligand. The introduction of Me and Et groups at the C-2 position of the propanoic acid of I further improved the PPARα-binding potency.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:199464 CAPLUS
DN 142:430102
TI Design, synthesis, and biological activity of novel PPARγ ligands based on rosiglitazone and 15d-PGJ2
AU Usui, Shinya; Suzuki, Takayoshi; Hattori, Yoshifumi; Etoh, Kazuma; Fujieda, Hiroki; Nishizuka, Makoto; Imagawa, Masayoshi; Nakagawa, Hidehiko; Kohda, Kohfuku; Miyata, Naoki
CS Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, Aichi, 467-8603, Japan
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(6), 1547-1551
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:430102
GI

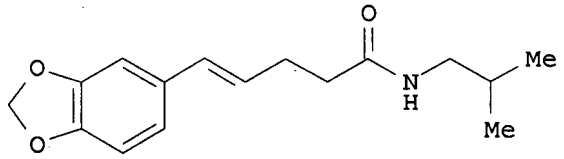


I

AB To develop novel PPARγ ligands, we synthesized thirteen 3-{4-(2-aminoethoxy)phenyl}propanoic acid derivs., which are designed based on the structures of rosiglitazone and 15d-PGJ2. Among these compds., compound I was found to be as potent as rosiglitazone in a binding assay and a preadipocyte differentiation test. Mol. modeling suggested that the nonyl group of I interacted with hydrophobic amino acid residues constructing the hydrophobic region of PPARγ protein where the alkyl chain of 15d-PGJ2 is expected to be located.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:394132 CAPLUS
DN 141:391898
TI Isolation and synthesis of isodihydropiperlonguminine
AU Anuradha, V.; Srinivas, P. V.; Rao, J. Madhusudana
CS Natural Products Laboratory, Organic Division-I, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SO Natural Product Research (2004), 18(3), 247-251
CODEN: NPRAAT; ISSN: 1478-6419
PB Taylor & Francis Ltd.
DT Journal
LA English
OS CASREACT 141:391898
GI



I

AB The hexane extract of dried fruits of Piper longum on fractionation afforded a new alkamide, isodihydropiperlonguminine(I) and two Ph propanoic acid derivs. The structures of these compds. are established based on spectroscopic evidence and synthesis.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:226581 CAPLUS
TI Novel dual PPAR α and γ agonists derived from 2-alkoxy-3-phenyl propanoic acid series, which ameliorates metabolic abnormalities and reduces body weight
AU Madhavan, G. R.; Chakrabarti, Ranjan; Reddy, Kalusam Anantha; Rajesh, B. M.; Rao, K. V. L. Narasimha; Rao, P. Bheema; Kumar, T. Ranjith;

Rajagopalan, R.
CS Metabolic Disorder Project Group, Dr. Reddy's Laboratories - Discovery Research, Hyderabad, 500050, India
SO Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-223 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69FGKM
DT Conference; Meeting Abstract
LA English
AB Obesity is a disorder of fat accumulation and is associated with several risk factors known as metabolic syndrome. Present therapeutic approach to obesity is therefore also focused on overall management of metabolic syndrome. Peroxisome proliferator activated receptor (PPAR) is a member of nuclear receptor super family. Two of its isoforms - PPARα and PPARγ are involved in the regulation of fat and carbohydrate metabolism and targets for hypolipidemic fibrates and antidiabetic thiazolidinediones. Considering the role of PPAR-α in catabolism of fat, we have initiated a program to discover a dual PPARα / γ-agonist with greater specificity towards PPAR-α, so that it can be used for improving metabolic syndromes and body weight gain. We have investigated 1, 3-Benzoxazine-4(3H)-one derivs. of 2-alkoxy-3-Ph propanoic acid derivs. The SAR contains Cl, NO2 , di-iso-Pr derivs. on aromatic ring of 1, 3-benzoxazinone and attachment of linker to -N' or -C' of the ring. Many compds. showed insulin sensitization and lipid lowering properties. DRF-2655 was selected as the lead mol. and resolved the racemic mixture in to its enantiomers (R and S). To our surprise both the enantiomers were having similar efficacy. Interestingly, DRF-2655 showed a significant body weight reduction in obese animal models along with good insulin sensitization and lipid lowering activity.

L1 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:226580 CAPLUS
TI New 2-ethoxy-3-(phenyl)propanoic acid derivatives as PPAR ligands
AU Bhuniya, Debnath; Iqbal, Javed; Chakrabarti, Ranjan; Mohan, Sankar; Narayanan, Sanju; Kumar, T. Ranjit; Suryaprakash, Raichur
CS Metabolic Disorder Group, Dr. Reddy-s Laboratories Ltd.- Discovery Research, Hyderabad, 500 049, India
SO Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-222 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69FGKM
DT Conference; Meeting Abstract
LA English
AB Peroxisome proliferators-activated receptor (PPAR) is being recognized as versatile target for managing metabolic syndromes. Glitazones, as PPAR-g agonist, and fibtares as PPAR-a agonists are in the market for treatment of insulin resistant type 2 diabetes and dyslipidemia resp. In order to address diabetes and dyslipidemia with a single mol., a PPAR-a/g dual acting compound has been conceptualized. We believe that a proper combination of a/g character may lead to a compound with such characteristics, without any significant PPAR-g related side effect. Along that line we have been working on design, synthesis and biol. evaluation of a series of 2-ethoxy-3-(phenyl)propanoic acids where Ph ring is linked through various spacers to a heterocycle. Quinazolinone as a representative heterocycle a general structure 1 with different examples have been screened on cell based PPAR assay. Selected compds. have been tested on relevant mice and rat models for type 2 diabetes and for dyslipidemia finally to come up with a lead structure having significant glucose and lipid lowering activity. Detailed synthesis and SAR will be presented in the form of poster.

L1 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:796655 CAPLUS

DN 139:292053
TI Etherification process for the preparation of 2-ethoxy-3-[4-[2-(4-methanesulfonyloxyphenyl)ethoxy]phenyl]propanoic acid derivatives
IN Larsson, Maria
PA Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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	WO 2003082812	A3	20040108		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU 2003226523	A1	20031013	AU 2003-226523	20030328
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	HK 1071353	A1	20061208	HK 2005-104064	20050513
PRAI	SE 2002-1005	A	20020402		
	WO 2003-GB1395	W	20030328		

OS CASREACT 139:292053; MARPAT 139:292053
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An efficient industrial-scale process for the preparation of 2-ethoxy-3-[4-[2-(4-methanesulfonyloxyphenyl)ethoxy]phenyl]propanoic acid derivs. [I; R = H, acid-protecting group; 1-(S)-2-ethoxy-3-[4-[2-(4-methanesulfonyloxyphenyl)ethoxy]phenyl]propanoic acid] is described which comprises the etherification of 2-ethoxy-3-(4-hydroxyphenyl)propanoate derivs. [II; e.g., Et (S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate] with 2-(4-methanesulfonyloxyphenyl)ethyl derivs. [III; X = leaving group; e.g., 2-(4-methanesulfonyloxyphenyl)ethyl methanesulfonate] in the presence of a base (e.g., sodium carbonate) and using water as a diluent.

L1 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:323168 CAPLUS
DN 120:323168
TI Dibasic (Amidinoaryl)propanoic Acid Derivatives as Novel Blood Coagulation

Factor Xa Inhibitors

AU Nagahara, Takayasu; Yokoyama, Yukio; Inamura, Kazue; Katakura, Shin-ichi; Komoriya, Satoshi; Yamaguchi, Hitoshi; Hara, Tsuyoshi; Iwamoto, Masahiro

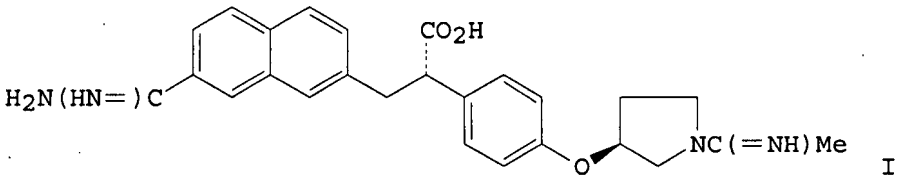
CS Research Institute, Daiichi Pharmaceutical Company Ltd., Tokyo, 134, Japan

SO Journal of Medicinal Chemistry (1994), 37(8), 1200-7
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

GI



I

AB Since activated factor X (FXa) is a coagulant enzyme that generates thrombin and participates in both intrinsic and extrinsic coagulation pathways, inhibition of FXa may be more effective than inactivation of thrombin for interrupting blood coagulation. To assess the possible effectiveness of FXa inhibition as an anticoagulant, the authors designed and synthesized 3-(amidinoaryl)-2-[4-[(3S)-3-pyrrolidinyloxy] phenyl]propanoic acid derivs. as low mol. weight, nonpeptidic, orally active FXa inhibitors. These derivs. exhibited potent and highly selective anti-FXa activity in vitro and anticoagulant activity on oral administration. The most promising compound, I, inhibited 50% of FXa activity (IC50) at 0.07 μM, doubled plasma recalcification time at 0.5 μM, and significantly prolonged activated partial thromboplastin time at 100 mg/kg oraly. In contrast with FXa inhibition, I showed no activity against thrombin (IC50 > 2000 μM).

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nested terms that are not separated by a logical operator.

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          1135 PPARS
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        492690 SUBSTITUTED
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       4311309 ACID
       1568117 ACIDS
       4812460 ACID
                 (ACID OR ACIDS)
        340439 DERIVATIVES
       1134482 DERIVS
       1240054 DERIVATIVES
                 (DERIVATIVES OR DERIVS)
L3           8 SUBSTITUTED PHENYLPROPANOIC ACID DERIVATIVES
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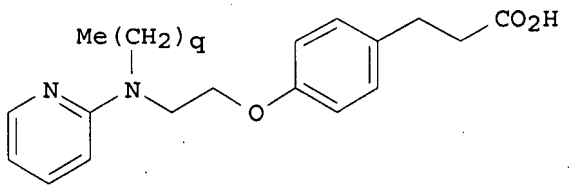
L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1170541 CAPLUS
DN 146:19381
TI Design, synthesis, and evaluation of a novel series of α-substituted phenylpropanoic acid derivatives as human peroxisome proliferator-activated receptor (PPAR) α/δ dual agonists for the treatment of metabolic syndrome
AU Kasuga, Jun-ichi; Yamasaki, Daisuke; Araya, Yoko; Nakagawa, Aya; Makishima, Makoto; Doi, Takefumi; Hashimoto, Yuichi; Miyachi, Hiroyuki
CS Institute of Molecular and Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo, 113-0032, Japan
SO Bioorganic & Medicinal Chemistry (2006), 14(24), 8405-8414
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
AB A series of α-alkyl-substituted phenylpropanoic acids was prepared as dual agonists of peroxisome proliferator-activated receptors alpha and delta (PPAR.alpha./δ). Structure-activity relationship studies indicated that the shape of the linking group and the shape of the substituent at the distal benzene ring play key roles in determining the potency and the selectivity of PPAR subtype transactivation. Structure-activity relationships among the amide series (10) and the reversed amide series (13) are similar, but not identical, especially in the case of the compds. bearing a bulky hydrophobic substituent at the distal benzene ring, indicating that the hydrophobic tail part of the mols. in these two series binds at somewhat different positions in the large binding pocket of PPAR. α-Alkyl-substituted phenylpropanoic acids of (S)-configuration were identified as potent human PPAR.alpha./δ dual agonists. Representative compds. exhibited marked nuclear receptor selectivity for PPAR.alpha. and PPAR.delta.. Subtype-selective PPAR activation was also examined by anal. of the mRNA expression of PPAR -regulated genes.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1341960 CAPLUS
DN 144:232775
TI Design and synthesis of substituted phenylpropanoic acid derivatives as human peroxisome proliferator-activated receptor α/δ dual agonists
AU Kasuga, Jun-Ichi; Makishima, Makoto; Hashimoto, Yuichi; Miyachi, Hiroyuki
CS Institute of Molecular and Cellular Biosciences, University of Tokyo, Tokyo, 113-0032, Japan
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 554-558
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB A series of phenylpropanoic acids was prepared as candidate dual agonists of peroxisome proliferator-activated receptors (PPAR) α and δ. Structure-activity relationship studies indicated that the shape of the linker moiety and the nature of the substituent at the distal benzene ring play key roles in determining the potency and selectivity of PPAR subtype transactivation. Optically active

α-ethylphenylpropanoic acid derivs. were identified as potent human PPAR α and δ dual agonists with potential for the treatment of metabolic syndrome.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:199464 CAPLUS
DN 142:430102
TI Design, synthesis, and biological activity of novel PPAR.gamma. ligands based on rosiglitazone and 15d-PGJ2
AU Usui, Shinya; Suzuki, Takayoshi; Hattori, Yoshifumi; Etoh, Kazuma; Fujieda, Hiroki; Nishizuka, Makoto; Imagawa, Masayoshi; Nakagawa, Hidehiko; Kohda, Kohfuku; Miyata, Naoki
CS Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, Aichi, 467-8603, Japan
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(6), 1547-1551
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:430102
GI

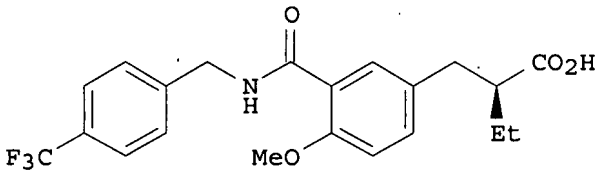


I

AB To develop novel PPAR.gamma. ligands, we synthesized thirteen 3-{4-(2-aminoethoxy)phenyl}propanoic acid derivs., which are designed based on the structures of rosiglitazone and 15d-PGJ2. Among these compds., compound I was found to be as potent as rosiglitazone in a binding assay and a preadipocyte differentiation test. Mol. modeling suggested that the nonyl group of I interacted with hydrophobic amino acid residues constructing the hydrophobic region of PPAR.gamma. protein where the alkyl chain of 15d-PGJ2 is expected to be located.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:524282 CAPLUS
DN 139:224182
TI Design, Synthesis, and Evaluation of Substituted Phenylpropanoic Acid Derivatives as Human Peroxisome Proliferator Activated Receptor Activators. Discovery of Potent and Human Peroxisome Proliferator Activated Receptor α Subtype-Selective Activators
AU Nomura, Masahiro; Tanase, Takahiro; Ide, Tomohiro; Tsunoda, Masaki; Suzuki, Masahiro; Uchiki, Hideharu; Murakami, Koji; Miyachi, Hiroyuki
CS Discovery Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi-chi, Shimotsugo-gun, Tochigi, 329-0114, Japan
SO Journal of Medicinal Chemistry (2003), 46(17), 3581-3599
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:224182
GI



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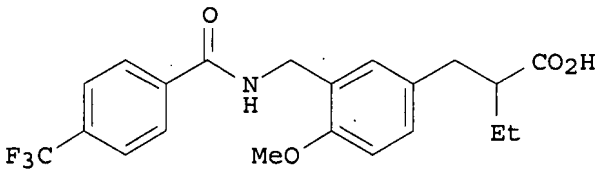

II

AB Substituted phenylpropanoic acid derivs. such as I are prepared as selective human peroxisome proliferator activated receptor α (PPAR.alpha.) activators. Structure-activity relationships for the binding of a variety of substituted phenylpropanoic acid derivs. to human peroxisome proliferator activated receptors are determined The nature and the stereochem. of the substituent at the α-position of the head part containing the carboxyl group, the distance between the carboxyl group and the central benzene ring, the linking group between the central benzene ring and the distal benzene ring, and the substituent at the distal hydrophobic tail part of the mol. all play key roles in determining the potency and selectivity of PPAR subtype transactivation. Mol. mechanics calcns. of the conformers of phenylpropanoic acid derivs. and of the enantiomers of an α-ethyl-substituted phenylpropanoic acid derivative are discussed. I is a particularly effective PPAR.alpha. activator with significant selectivity for PPAR.alpha.. In rats, I decreases serum cholesterol and lipids over five days of administration in a dose-dependent manner and with a significantly greater efficacy than a representative fibrate (bezafibrate) used for comparison. Phenylpropanoic acid II is found to be a dual activator of PPAR.alpha. and of PPAR.delta..

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:184227 CAPLUS
TI Design, synthesis, and evaluation of substituted phenylpropanoic acid derivatives as human peroxisome proliferator-activated receptor activators: The discovery of potent and human PPAR subtype-selective activators
AU Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro; Ide, Tomohiro; Tsunoda, Masaki; Suzuki, Masahiro; Nagasawa, Michiaki; Uchiki, Hideharu; Murakami, Koji
CS Discovery Research Laboratories, Kyorin Pharmaceutical Co., Ltd, Tochigi, 329-0114, Japan
SO Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), MEDI-261 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69DSA4
DT Conference; Meeting Abstract
LA English
AB A series of phenylpropanoic acids was prepared as part of a search for subtype-selective PPAR alpha activators. SAR studies indicated

that the nature of the substituent at the alpha position of the head part containing the carboxyl group, the distance between the carboxyl group and the central benzene ring, the linking group between the central benzene ring and the distal benzene ring, and the substituent at the distal hydrophobic tail of the mol. all play key roles in determining the potency and the selectivity. Transactivation study using chimeric PPAR alpha indicated that species-selective PPAR alpha transactivation was mediated via the interaction between the activator and the side chain of a crucial amino acid located in the helix three region of PPAR alpha. This study has led to the identification of potent and human PPAR alpha-selective derivs., which will be useful as candidate drugs for the treatment of metabolic disorders.

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:900080 CAPLUS
DN 136:318816
TI Design, synthesis and evaluation of substituted phenylpropanoic acid derivatives as peroxisome proliferator-activated receptor (PPAR) activators: novel human PPAR.alpha.-selective activators
AU Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro; Takahashi, Yukie; Ide, Tomohiro; Tsunoda, Masaki; Murakami, Koji; Awano, Katsuya
CS Kyorin Pharmaceutical Co., Ltd., Discovery Research Laboratories, Tochigi, Shimotsuga-gun, Nogi-machi, 329-0114, Japan
SO Bioorganic & Medicinal Chemistry Letters (2001), Volume Date 2002, 12(1), 77-80
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 136:318816
AB A series of substituted phenylpropanoic acid derivs. was prepared as part of a search for subtype-selective human peroxisome proliferator-activated receptor (PPAR) activators. Structure-activity relationship studies indicated that the substituent at the α-position of the carboxyl group plays a key role in determining the potency and the selectivity for PPAR transactivation.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:284304 CAPLUS
DN 135:57906
TI Fluorine-Substituted Ligands for the Peroxisome Proliferator-Activated Receptor Gamma (PPAR.gamma.): Potential Imaging Agents for Metastatic Tumors
AU Kim, Sung-Hoon; Jonson, Stephanie D.; Welch, Michael J.; Katzenellenbogen, John A.
CS Department of Chemistry, University of Illinois, Urbana, IL, 61801, USA
SO Bioconjugate Chemistry (2001), 12(3), 439-450
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB The peroxisome proliferator-activated receptor gamma (PPAR γ), a primary regulator of lipid metabolism, is present in many tumor cell lines and animal tumor systems and, in some cases, can mediate effective antitumor therapy with potent synthetic ligands. In an approach to image tumors with positron-emission tomog. (PET) based on their content of PPAR.gamma., we have synthesized two fluorine-substituted analogs of a high affinity ligand from the phenylpropanoic acid class. The analog having the highest affinity for PPAR.gamma. was labeled with the positron-emitting radionuclide fluorine-18. In tissue distribution studies in normal rats and in SCID mice bearing human breast tumor xenografts, this compound did not show evidence of receptor-mediated

uptake. The prospects for using PPAR.gamma. as a target for imaging tumors may be limited by the low receptor concns. in tumors and by the pharmacokinetic behavior of this class of ligands, which appears to be more favorable for therapy than for imaging.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
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NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role

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NEWS 14   DEC 18  CA/CAplus patent kind codes updated
NEWS 15   DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                  to 50,000
NEWS 16   DEC 18  MEDLINE updated in preparation for 2007 reload
NEWS 17   DEC 27  CA/CAplus enhanced with more pre-1907 records
NEWS 18   JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19   JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20   JAN 16  IPC version 2007.01 thesaurus available on STN
NEWS 21   JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22   JAN 22  CA/CAplus updated with revised CAS roles
NEWS 23   JAN 22  CA/CAplus enhanced with patent applications from India
NEWS 24   JAN 29  PHAR reloaded with new search and display fields
NEWS 25   JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases

NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
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DICTIONARY FILE UPDATES:   8 FEB 2007  HIGHEST RN 920112-67-0

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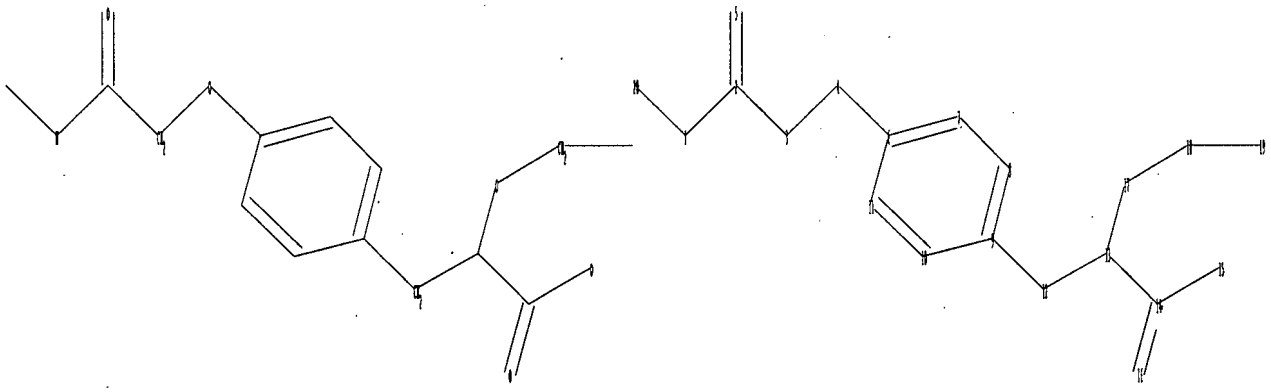

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6 7 8 9 10 11
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18-19
ring bonds :
6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-20 2-5 4-6 13-17 14-15 14-16
exact bonds :
2-3 3-4 9-12 12-13 13-14 17-18 18-19
normalized bonds :
6-7 6-11 7-8 8-9 9-10 10-11

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom
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L3 QUE L2 AND L1

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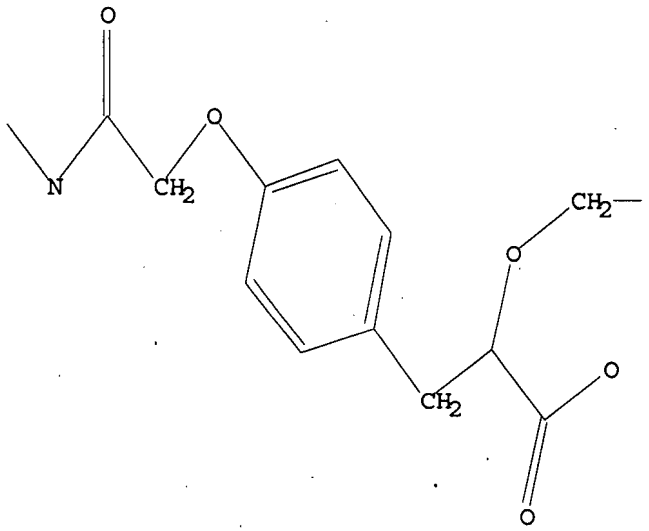

Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED     4810 ITERATIONS                                 123 ANSWERS
SEARCH TIME: 00.00.01

L4          123 SEA SSS FUL L2

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COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.10     172.31

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REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
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SAMPLE SCREEN SEARCH COMPLETED - 255 TO ITERATE

100.0% PROCESSED 255 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4142 TO 6058
PROJECTED ANSWERS: 5 TO 234

L5 5 SEA SSS SAM L2

L6 5 L5

=> d L6 1-5 bib abs

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:61504 CAPLUS
DN 146:142376
TI Preparation of phenylpropionic acid derivatives and pharmaceutical compositions thereof
IN Bjoerk, Seth
PA Astrazeneca AB, Swed.
SO PCT Int. Appl., 57pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007008156	A1	20070118	WO 2006-SE864	20060710

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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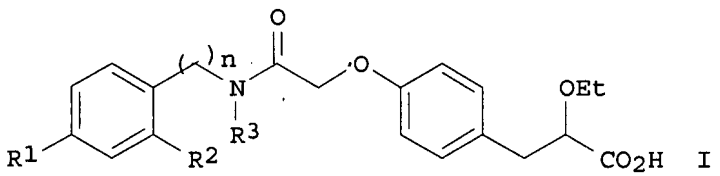

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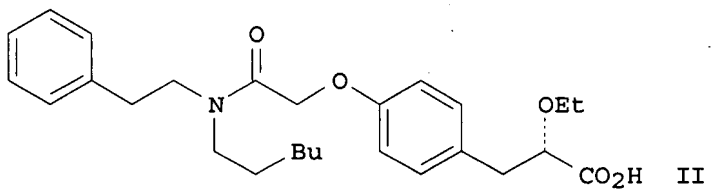

II

AB The title phenylpropionic acid derivs. I [wherein n = 1-2; R1 = H, Cl, CF3, or OCF3; R2 = H or F; R3 = alkyl] or tert-butylamine salts thereof were prepared as PPAR active compds. for treatment of metabolic syndrome including type 2 diabetes mellitus (no data). For example, II and II•tert-butylamine were prepared in a multi-step synthesis. Pharmaceutical compns. were described.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1335635 CAPLUS
DN 144:69628
TI Preparation of phenoxyacetamide derivatives as modulators of peroxisome proliferator-activated receptors (PPAR)
IN Alstermark, Eva-Lotte Lindstedt; Olsson, Anna Christina; Li, Lanna
PA Swed.
SO U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 499,261.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

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	WO 2003051821	A1	20030626	WO 2002-GB5738	20021218
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WO 2004056748 A1 20040708 WO 2003-GB5602 20031219
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WO 2004113270 A2 20041229 WO 2004-EP6597 20040617
WO 2004113270 A3 20050331
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EP 1676833 A1 20060705 EP 2006-5766 20040617
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JP 2005336209 A 20051208 JP 2005-235794 20050816
JP 2006045240 A 20060216 JP 2005-253346 20050901
JP 2006298924 A 20061102 JP 2006-123399 20060427
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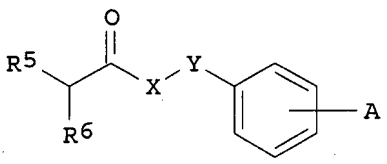
PRAI SE 2001-4334 A 20011219
WO 2002-GB5738 W 20021218
WO 2002-GB5744 A 20021218
GB 2002-29931 A 20021221
GB 2003-14079 A 20030618
WO 2003-GB305602 A 20031219
WO 2004-EP6597 A 20040617
US 2005-499261 A2 20050304
CN 2002-828123 A3 20021218
JP 2003-552709 A3 20021218
JP 2003-552710 A3 20021218
JP 2004-561668 A3 20031219
EP 2004-740044 A3 20040617
JP 2006-515989 A3 20040617
OS MARPAT 144:69628
GI



I

AB The phenyl-, phenoxy-, or phenylthioalkanamidetitle compds., (in particular phenoxyacetamide derivs.) (I) [A is situated in the ortho, meta or para position and represents CR3R4CR1R2COR, CR3:CR1COR (wherein R = H, alkyl, (un)substituted HO or NH2; R1 = alkyl, aryl, alkenyl, alkynyl, or when A is CR3R4CR1R2COR, R1 can also be cyano, (un)substituted HO, SH, OCONH2, SO2NH2, CO2H, etc.; R2 = H, halogen, alkyl, aryl, alkylaryl; R3, R4 = H, alkyl, aryl, alkylaryl); Y = O, S, a single bond; n = an integer

of 1-4; X = alkyl; R5, R6 = H, each (un)substituted C1-13 alkyl, C2-10 alkenyl, or C2-10 alkynyl; or R5, R6 = each (un)substituted C3-8 cycloalkyl, C3-C8 cycloalkenyl, aryl, heterocyclyl, or heteroaryl; or R5 and R6 together with the nitrogen atom to which they are attached form a single or a fused heterocyclic system] are prepared These compds. are useful in treating clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance, and other manifestations of the metabolic syndrome. Thus, a solution of 0.598 g N-butyl-N-[2-fluoro-4-(trifluoromethyl)benzyl]amine and 0.593 g [4-((2S)-2,3-diethoxy-3-oxopropyl)phenoxy]acetic acid in 20 mL CH2Cl2 was treated with 0.80 mL N,N-diisopropylethylamine and 0.674 g O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate and the reaction mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., 74% Et (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate (II). A solution of 0.748 g II in 70 mL MeCN was treated with 35 mL 0.10 M LiOH and the reaction mixture was stirred at room temperature overnight, neutralized with 5% HCl, concentrated, acidified with 5% HCl, and extracted with
EtOAc to give 97% (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid (III). III showed EC50 of 0.001 μmol/L for human PPARα.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1154649 CAPLUS
DN 142:93514
TI Preparation of phenylpropanoic acid derivatives as PPARα agonists
IN Li, Lanna; Lindstedt-Alstermark, Eva-Lotte; Olsson, Christina
PA Astrazeneca Ab, Swed.
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

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	WO 2004113270	A3	20050331		
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	AU 2004249409	A1	20041229	AU 2004-249409	20040617
	CA 2528234	A1	20041229	CA 2004-2528234	20040617
	US 2005148656	A1	20050707	US 2003-518777	20040617
	EP 1675820	A2	20060705	EP 2004-740044	20040617
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	EP 1676833	A1	20060705	EP 2006-5766	20040617
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	BR 2004011484	A	20060725	BR 2004-11484	20040617
	CN 1835913	A	20060920	CN 2004-80023304	20040617
	JP 2006527730	T	20061207	JP 2006-515989	20040617
	US 2005282822	A1	20051222	US 2004-26806	20041230
	NO 2005005892	A	20060106	NO 2005-5892	20051212
	JP 2006298925	A	20061102	JP 2006-139673	20060519
	US 2006258866	A1	20061116	US 2006-477168	20060628

PRAI	GB 2003-14079	A	20030618
	SE 2001-4334	A	20011219
	WO 2002-GB5738	W	20021218
	WO 2002-GB5744	A	20021218
	GB 2002-29931	A	20021221
	WO 2003-GB305602	A	20031219
	EP 2004-740044	A3	20040617
	JP 2006-515989	A3	20040617
	WO 2004-EP6597	W	20040617
	US 2005-518777	A3	20050303
	US 2005-499261	A2	20050304

OS MARPAT 142:93514

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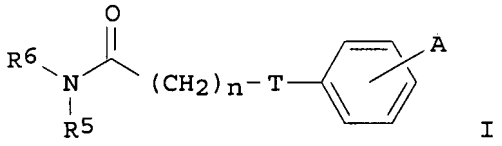

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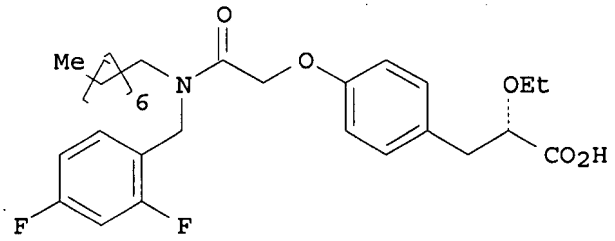

II

AB Title compds. represented by the formula I [wherein A = CR3(R4)CR1(R2)COR or C(R3):C(R1)COR; R = H, alkoxy, (alkyl)aryloxy, amino, etc.; R1 = alkyl, aryl, alkenyl, alkynyl, etc.; R2 = H, halo, alkyl, (alkyl)aryl; R3, R4 = independently H, alkyl, (alkyl)aryl; T = O, S or a single bond; n = 1-4; R5, R6 = independently selected substituent comprising C, H, N, O, S, Se, P or halo; with provisos; optical isomers and racemates thereof as well as pharmaceutically acceptable salts, prodrugs, solvates and crystalline forms thereof] were prepared as PPARα agonists. For example, II was given in a multi-step synthesis starting from the reaction of 2,4-difluorobenzylamine with octanoic acid. I had EC50 values of less than 0.1 μmil/L for PPARα and showed the ration of the EC50(PPARγ) with EC50(PPARα) is greater than 150:1. Thus, I and their pharmaceutical compns. are useful for the treatment of clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance (no data).

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:2837 CAPLUS

DN 140:59411

TI Preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X

IN Ferritto Crespo, Rafael; Martin, Jose Alfredo; Martin-Ortega, Finger Maria Dolores; Rojo Garcia, Isabel; Shen, Quanrong; Warshawsky, Alan M.; Xu, Yanping

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000789	A1	20031231	WO 2003-US16207	20030611
	WO 2004000789	A9	20040311		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2488972	A1	20031231	CA 2003-2488972	20030611
	AU 2003241579	A1	20040106	AU 2003-241579	20030611
	EP 1517882	A1	20050330	EP 2003-731326	20030611
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	BR 2003011834	A	20050412	BR 2003-11834	20030611
	CN 1662487	A	20050831	CN 2003-814173	20030611
	JP 2005529975	T	20051006	JP 2004-515700	20030611
	US 2006111406	A1	20060525	US 2004-517581	20041208
PRAI	US 2002-390102P	P	20020619		
	WO 2003-US16207	W	20030611		

OS MARPAT 140:59411

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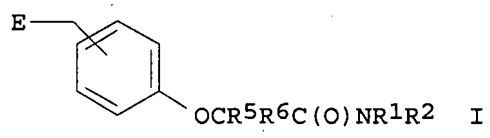

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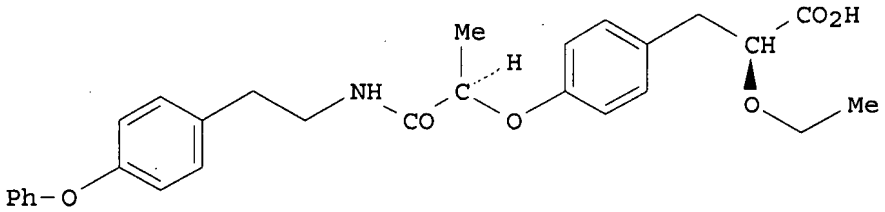

II

AB The present invention is directed to phenoxyalkanamides (shown as I; variables defined below; e.g. II), compns., and their use as peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X. The binding and cotransfection efficacy values found for compds. of this invention that are useful for modulating a PPARα receptor are about <100 nM and >50%, resp. Although the methods of preparation are not claimed, .apprx.140 example prepns. of I are included. For example, II was prepared in 3 steps starting from (2S)-2-ethoxy-3-(4-hydroxyphenyl)propionic acid Me ester, (2S)-2-hydroxypropionic acid benzyl ester and involving intermediates (2S)-3-[4-[[(1R)-1-[(benzyloxy)carbonyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid Et ester and (2S)-3-[4-[((1R)-1-carboxyethyl)oxy]phenyl]-2-ethoxypropionic acid. For I: R1 = H, C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-4-alkyl, heteroaryl-C0-4-alkyl, aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-2-alkyl, arylheteroC1-C8alkyl, -CHC(O)C1-C4 alkoxy, C0-4-alkyl-C(O)heteroC1-C8alkyl, and -CH2C(O)-R15R16. R2 = C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, heteroC1-C6cycloalkylaryl, heteroC1-C6cycloalkylarylC1-C4alkyl,

aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-C2-alkyl, arylheteroC1-C8alkyl, C0-C4-alkyl-C(O)heteroC1-C8alkyl, -CH(C(O)OCH3)benzyl, and -CH2C(O)R15''R16''. R1 and R2 together may form a heterocyclic ring which heterocyclic ring is (un)substituted with 1-3 substituents R1' and which heterocyclic ring is optionally fused with an aryl; E = C(R3)(R4)A, (CH2)nCOOR13, aryl-C0-C4-alkyl, thio-C1-C4-alkyl, thioaryl, arylC1-C4alkoxy, C1-C4alkoxy C1-C4alkyl, aminoaryl, and aminoC1-C4alkyl. R5 and R6 = H, C1-C8 alkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, C3-C6 cycloalkyl, aryl-C0-C2-alkyl, C3-C6 cycloalkyl-C0-2-alkyl, and -CH2C(O)R17R18.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:491168 CAPLUS
DN 139:69049
TI Preparation of substituted phenylpropionic acid derivatives as agonists to human peroxisome proliferator-activated receptor alpha (PPAR)
IN Alstermark Lindstedt, Eva-Lotte; Olsson, Anna Christina; Li, Lanna
PA Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003051821	A1	20030626	WO 2002-GB5738	20021218
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	CA 2470491	A1	20030626	CA 2002-2470491	20021218
	AU 2002366315	A1	20030630	AU 2002-366315	20021218
	EP 1458673	A1	20040922	EP 2002-804964	20021218
	EP 1458673	B1	20060906		
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	BR 2002014988	A	20041214	BR 2002-14988	20021218
	HU 200402133	A2	20050228	HU 2004-2133	20021218
	CN 1620422	A	20050525	CN 2002-828123	20021218
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	US 2005171204	A1	20050804	US 2003-499261	20021218
	JP 2005526011	T	20050902	JP 2003-552709	20021218
	JP 3784804	B2	20060614		
	TW 253444	B	20060421	TW 2002-91136518	20021218
	NZ 533276	A	20060428	NZ 2002-533276	20021218
	TW 255807	B	20060601	TW 2002-91136519	20021218
	AT 338743	T	20060915	AT 2002-804964	20021218
	CN 1896045	A	20070117	CN 2006-10007173	20021218
	ZA 2004004657	A	20050829	ZA 2004-4657	20040611
	ZA 2004004658	A	20060222	ZA 2004-4658	20040611
	NO 2004003023	A	20040715	NO 2004-3023	20040715
	US 2005282822	A1	20051222	US 2004-26806	20041230
	JP 2005336209	A	20051208	JP 2005-235794	20050816
	JP 2006298924	A	20061102	JP 2006-123399	20060427
PRAI	SE 2001-4334	A	20011219		
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	JP 2003-552710	A3	20021218
	WO 2002-GB5738	W	20021218
	WO 2002-GB5744	A	20021218
	GB 2002-29931	A	20021221
	GB 2003-14079	A	20030618
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	WO 2004-EP6597	A	20040617
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OS MARPAT 139:69049

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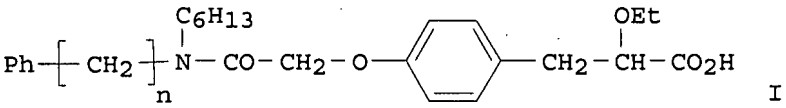

I

AB The S enantiomer of I, n = 1 or 2, (C6H13 = hexyl) as well as their pharmaceutically acceptable salts, solvates, crystalline forms and prodrugs are synthesized using various solvents and in presence of charcoal-supported palladium catalyst. The utility of these compds. in clin. conditions such as lipid disorders (dyslipidemias) whether or not associated with insulin resistance and therapeutic and other pharmaceutical activities is also investigated. For example, (2S)-3-(4{2-[benzyl(hexyl)amino]-2-oxoethoxy}phenyl)2-ethoxypropionic acid was prepared in 58% yield via reaction of (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate and benzyl bromoacetate.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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